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Developing the Framework for an Epidemic Forecast Infrastructure

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3rd FFCUL Progress Report

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Work package participants

The following partners have taken active part in the work leading to the elaboration of this document, even if they might not have directly contributed writing parts of this document:

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- Livia Moreira
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Change log

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1.1	**2010.09.13**	**ns**	**Updated CMAF report**
1.0.1	**2010.09.06**	**mjs**	**Incorporated XLDB Team feddback**
1.0	**2010.09.01**	**mjs**	**Created**

Executive Summary

The report includes a summary of the work carried out by FFCUL in the third semester of the project.

FFCUL Progress Report 2010.02.01 to 2010.07.31

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15th of September 2010

Abstract

The report includes a summary of the work carried out by the LASIGE group of FFCUL in the reporting period, the third semester of the project life. The work by the CMAF group of FFCUL in WP1 is reported in a separate document.

Keyword List: progress-report, third-semester

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1 Overview

The Epiwork project started in February 2009 and will run for 48 months. This report summarises the progress in the third semester of the project activity by the LASIGE Group of FFCUL.

According to the work plan FFCUL is involved in the following work packages:

WP 1 Population Models and Contact Networks

WP 3 Information platform

WP 4 Epidemic Modelling Platform

WP 7 Management

The FFCUL participation in Epiwork involves two groups:

- CMAF Group
- LASIGE Group

1.1 LASIGE Group Roster

The LASIGE Team working on WP3 and W4 in this period includes:

- Mário J. Silva (FCUL Faculty, worked in the reporting period in WP3, WP4 and WP7)
- Fabrício Silva (FCUL Faculty, worked in the reporting period in WP3 and WP4 – Left FFCUL at the end of July 2010)
- Francisco Couto (FCUL Faculty, worked in the reporting period in WP3)
- Dulce Domingos (FCUL Faculty, worked in the reporting period in WP3 – started in May/2010)
- Luís Filipe Lopes (Post-doc researcher+Master Student, worked full-time during the reporting period).

- Hugo Ferreira (Master student, worked full-time in the reporting period).
- Carla Patrícia Sousa (Master student, worked 60%-time in the reporting period).
- Graduate student João Zamite (Master student, worked full-time in the reporting period).

There is a discrepancy in the profiles of the people hired to work on Epiwork at LASIGE and the initially planned, the reason being that we were unable to fill the software engineer and a post-doc positions as planned, with previous directly related experience and salaries matching our budget.

As a result, we have been using Informatics Engineering and Biomedical Informatics students on the infrastructure setup assisted by FCUL faculty and senior technical staff. LASIGE has hired more people in the first at a reduced cost, which was the contingency measure found to manage the situation.

Meanwhile, Fabrício Silva and Hugo Ferreira announced that they would leave the project at the end of July 2010, and Luís Lopes at the end of October 2010.

We have now Prof. Dulce Domingues joining the project. She will be mainly addressing data privacy issues in the epidemic marketplace, together with João Zamite, who will be advised on his PhD by her.

We have hired a new Master student in Communication Design, Juliana Duque, who will work in the project for one year in the design of the user interfaces for a second version of the Epidemic Marketplace, starting in September.

2 Work in WP1 — Population Models and Contact Networks

The CMAF group of FFCUL is participating in this task and sending a separate progress report.

3 Work in WP3 — Information platform

This task is lead by FFCUL, with a total contribution of 82 persons.month (60 hired technicians + (22) academics).

3.1 Background Information on WP3

Work package number	3		**Start date or starting event:**		Month 1		
Work package title	**Information platform**						
Activity type	RTD						
Participant number	12	1	2	3	4	5	9	10
Participant short name	FFCUL	ISI	FGC-IGC	TAU	MPI-DS	AIBV	BIU	FBK-IRST
Person-months per participant	82	60	4	8	42	2	11	6

The whole WP3 activity is structured into four tasks:

Task 3.1 – Data Collection.

Participants: FFCUL, ISI, FBK-IRST, BIU, MPI-DS, FGC-IGC, AIBV.

Description: Realistic simulations of epidemic processes crucially depend on the availability of datasets describing human behaviour and pathogen-host interactions. Datasets include population movement data, social and behavioural data, health related data, geographic data, detailed geo-temporal epidemic incidence and immunization data, pathogen evolution and multi-strains circulation data. Data can come from a variety of different sources, including hospital records, country statistics, Web content, and others. It can range from a global scale, such as the worldwide air transportation infrastructure, down to the

detailed description of individual activities at a minute-by-minute scale. This task will create a catalogue of databases of epidemiological data across Europe, with extensive meta-data describing the main characteristics of the available information sources. This catalogue will be integrated with a collaborative platform that will be set up for online discussion and exchange of meta-data among the participants.

Task 3.2 – Meta-Model Design.

Participants: FFCUL, IGC, ISI.

Description: While some of the previously mentioned datasets are freely available on the Web (e.g. WHO Global Health Atlas, Eurostat), they are often scattered in different repositories, cover partial regions of the world and come in different formats, according to different standards and classifications. The project envisions a unified and integrated approach for the management of these resources, with the design and implementation of an Epidemic Marketplace Platform, publicly available on the web. The platform supports the sharing and management of epidemic datasets and resources as well as their rating, annotation, and selection. It is an on-line social networking site that will serve researchers, practitioners, and educators all over the world to foster a virtual community for epidemic research. It will support the exchange of resources as well as user interactions. Based on a Web2.0 approach, users will become active participants, sharing information and data, and collaborating online, rather than being satisfied with a passive information consumer/viewer role. We envision proposing a simple reference format, which will facilitate the navigation and use of the datasets. Each dataset will come with a metadata file, signalling general metadata for resource management, containing data such as: the title, the date of submission, version, the source of the data and coverage. Moreover, the metadata will include information for a more thorough description of the data included in the dataset, providing a framework for a more specific description, for example, of epidemiologic and geographic data,. The Marketplace will support flexible and intuitive tools for navigation and selection of resources.

Standard classifications as well as tagging systems proposed by users will be supported.

Task 3.3 – Epidemic Marketplace Platform.

Participants: FFCUL, ISI.

Description: This task will implement a platform based on the integration of grid technology and publicly available services and software on the web to support the sharing and management of epidemic datasets and resources as well as their rating, annotation, and selection. The Epidemic Marketplace Platform will be an on-line social networking site that will serve researchers, practitioners, and educators all over the world to foster a virtual community for epidemic research. It will support the exchange of resources as well as user interactions. Based on some of the Web2.0 characteristics, users will become active participants, generating information and providing data for sharing, and collaborating online, rather than being satisfied with a passive information consumer/viewer role. More specifically, researchers can use and contribute to the Marketplace in several different ways. They can: (1) use it as a catalogue of data sources containing the metadata describing existing databases; (2) view, download, tag, and comment on the available resources; (3) provide compliant datasets and relevant information; (4) use it as a forum where to publish information about their own data, seek modellers to collaborate with, share and distribute their new findings.

Task 3.4 – Evaluation and monitoring of the use of the catalogue and collaboration services.

Participant: FFCUL.

Description: This task involves the monitoring of epidemiological data exchanges performed through the mediating services platform. The evaluation will assess not only the coverage of the catalogued resources, but the users‘ satisfaction with the user interface and integrated collaborative tools made available through the epidemiological marketplace platform. More importantly, the analysis of the collected datasets and their annotations and usage will

provide a rich environment for deriving an epidemiology ontology, which will help further on the integration and communication among the community of epidemiologists.

3.2 Progress in the Reporting Period

As in the first year, the work done by the LASIGE Team in the reporting period was related to Task 3.1, Task 3.2 and Task 3.3. Evaluation work in Task 3.4 will start once the information platform is deployed.

Main Activities at FFCUL in the third semester of the project in this work package:

1. Mário Silva and Fabrício Silva attended the Epiwork Review in Brussels in March – Mário Silva presented the two completed WP3 deliverables to the EC and gave an overview of the progress and challenges in WP3.The demo of the fully functional Epidemic Marketplace prototype was presented to the reviewers, who had the opportunity to obtain user accounts for browsing the EM repository and forum.
2. Mário Silva and Fabrício Silva attended the COSI-ICT cluster workshop in Brussels, March 2010
3. Francisco Couto participated in the VPH-OBO ontology workshop at Cambridge UK for knowing relevant case studies and guidelines in ontology development in the biomedical field. During the workshop, Francisco discussed with Barry Smith (National Center for Ontological Research, USA) the state of the art of epidemiological ontologies and a possible collaboration within the IDO (infectious disease ontology).
4. Metadata model refinement, identification of relevant ontologies for annotation and development of a metadata editor for the repository embodying the proposed model.
5. Implementation of mediator services in the EM, handling issues with REST services organization and authentication, OAI-PMH support.

6. Mário Silva attended WP5 Meeting in Amsterdam in May; presentation by Mário Silva and discussions on the Integration and privacy issues regarding collected data on WP3/WP5.
7. Major reorganization of the base software infrastructure, which is now entirely deployed in various virtual machines hosted in the two servers dedicated to the Epidemic Marketplace.
8. Development of a second version of a data collector proceeded for deployment at September 30th.
9. Development of the initial Epidemic Marketplace mediator services continued and their release is planned on September 30th. There were some issues related to the format of service requests and results, regarding the incompatibilities of two main requirements: adoption of the REST syntax and OAI-PMH.
10. Development of the metadata editor for epidemic datasets, implementing the policies outlined in deliverable D3.1 nearly completed.
11. Evaluation of Integration of Drupal with Fedora Commons, using the Islandora module extension to Drupal and using this software as basis for a new version of the Repository/Forum of the Epidemic Marketplace.

Publications and Presentations:

1. Fabrício A.B. Silva, Mário J. Silva, Francisco Couto 2010: Epidemic Marketplace: an e-Science Platform for Epidemic Modelling and Analysis. ERCIM News 82 - Special Theme: Computational Biology.
2. Luis Filipe Lopes, Fabrício A.B. Silva, Francisco Couto, João Zamite, Hugo Ferreira, Carla Sousa, Mário J. Silva, Epidemic Marketplace: An Information Management System for Epidemiological Data. Presented at ITBAM'10 - 1st International Conference on Information Technology in Bio- and Medical Informatics - DEXA 2010 - August, 2010.
3. João Zamite, Fabrício A.B. Silva, Francisco Couto, Mário J. Silva, MEDCollector: Multisource Epidemic Data Collector. Presented at

ITBAM'10 - 1st International Conference on Information Technology in Bio- and Medical Informatics - DEXA 2010 - August, 2010.

4. Mário J. Silva, Fabrício A.B. Silva, Luís Filipe Lopes, Francisco Couto, Building a Digital Library for Epidemic Modelling. Proceedings of ICDL 2010 - The International Conference on Digital Libraries 1, p. 447--459, New Delhi, India, 23--27 February, 2010. TERI Press -- New Delhi, India. Presentation of invited paper.,
5. Presentation in Brussels 2nd and 3rd, 2009. (http://www.epiwork.eu/2009/02/03/kickoff-meeting-of-the-epiwork-project/)
6. Presentation in Amsterdam, WP5 second meeting, May, 2010. (http://www.epiwork.eu/2009/06/05/first-epiwork-wp5-meeting-in-amsterdam-25-26th-of-may-2009/).
7. Presentation and demo of EPIWORK to students at the University of Valencia, Spain in an invited 4hrs seminar, by Fabricio Silva
8. Presentation of EPIWORK to students of the Master/Phd in Epidemiology at the Faculty of Medicine of the University of Lisbon, in an invited 3h seminar, by Mario Silva.

Activities at FFCUL in the third semester of the project in Task 3.1:

The data collection activity started at the end of the first year. We have been automatically collecting the following data with the MedCollector since then, from the following sources:

- Messages from Twitter containing disease names and posted at each country or capital of the world.
- Google Flu Trends Datasets.
- RSS Feeds from the CDC. Including travel notices alerts and emerging diseases alerts.
- Email Newsletter messages from ProMEDmail.

Activities at FFCUL in the third semester of the project in Task 3.2:

Work in this task included:

- Population of the repository with datasets and resources found relevant to epidemic modellers gathered from the Web, used for validation of the metadata modelling decisions.
- Development of a metadata editor for epidemic datasets for the EM platform, following the policies outlined in deliverable D3.1.

Activities at FFCUL in the third semester of the project in Task 3.3:

- Reconfiguration of the infrastructure, now based on virtual machines. Configuration of the production and development environments for the Lisbon EM node.
- Deployment of a new version of the EM base software, to be based in Fedora Commons version 3.0 and the Drupal Content Management System, initiated in January continued. This new version will substitute the current, based on Fedora Commons 2.2.2 and Muradora 1.3.3. This new version is planned to replace the production environment of the EM in 2011.
- The first operational prototype of the Epidemic Marketplace was presented in the March 2010 review in Brussels, and made available to reviewers since then from http://epiwork.di.fc.ul.pt.
- Discussions with partners involved in WP3 on how to identify relevant datasets to the catalogue and strategies and incentives for populating the Epidemic Marketplace.

Activities at FFCUL in the third semester of the project in Task 3.4:

- Continued work on planning of the monitoring and log data collection and analysis tasks. Actual collection of usage data will start once the initial system is fully deployed.

3.3 Effort Allocation

The effort allocated to WP3 in the reporting period is as follows:

WP3 FFCUL **Reporting Period**	**Effort** (p.m) Non-Perm + Perm =Total
Year 1: February 1, 2009 to January 31, 2010	19.38 + 4.53 = 23.91
Semester 3: February 1, 2010 to July 31, 2010	18.30 + 2.61 = 20.91

The commitment to the project in the first year was 23.91 persons.month, 19.38 pm from technicians, and 4.53 p.m from permanent staff.

In the reporting period (3rd semester), the commitment was 20.91 persons.month, 18.30 pm from technicians, and 2.61 p.m from permanent staff

This is now well above planned (assuming a 10.25 p.m constant effort/semester), and reflects the decision of hiring more (and less skilled) staff for the FFCUL/LASIGE team of Epiwork in Semester 2.

3.4 Outcast for WP3

Focus for the 2nd year will be on providing the methods to achive **INTEGRATION** with the EPIWORK partner's systems and tools.

The revised outcast for WP3 is outlined in the updated SWOT analysis chart, shown below:

Epidemic Marketplace SWOT Analysis

Strengths	**Weaknesses**
• Epiwork-driven EM • Standards-based • Open Source modules	• Consortium enters "everyone for himself" mode. • "Somebody will take care of that" attitude

• Supported (until 2013)	• Interfaces to WP4 and WP5? • Compelling scenario? • Someone turning EM into a very expensive complex and useless cache (not likely)
Opportunities • Epiwork testbed • Creation of a baseline for epidemic modelling • Showcase for partners' outputs	**Threats** • Unpopulated EM • What are the incentives?

Some of the activities that we plan to undertake until deliverable D3.3 is released at the end of September 2010 are:

- Populate the Repository with information that will make it an useful tool to the epidemic modelers community: this is at least in part being accomplished because we have been working with ISI on having all the data files used by the GLEaM – Global Epidemic and Mobility – modeler developed by the ISI.
- Publish the EM Middleware APIs
- Make a software release of all the software and configuration data of the first version of the EM.

We have decided not to replace Muradora and the phpBB forum, by the Drupal Content Management System in the version to be released by September 30, because the user interface is not developed and we are not as confident about its reliability as we wanted.

Later on, the envisaged activities will mainly involve:

- Redesigning the user interface of the EM.

- Moving to having version 2.0 of the Epidemic Marketplace (Drupal/Islandora/Fedora Commons 3-based) in production
- Continuing work on populating and documenting the EM Repository.
- Addressing access control for data sharing within the community of epidemiologists, and Ethics, Privacy and Anonymization issues that must be tackled by the Epidemic Marketplace before it is publicly announced – João Zamite is starting his PhD under supervision of Dulce Domingos on this theme.
- Incorporating in the systems of project partners a Distributed Authentication and Access control mechanism.
- Providing tools for selecting datasets or parts of the information thereof from the EM collection for retrieval access by epidemic modelling tools.
- Replicating the Lisbon EM node at another partner.
- Review current work on epdimiological ontologies towards the development of ontological integrative approach that will help further on the integration and communication among the community of epidemiologists

4 Work in WP4 — Epidemic Modelling Platform

This task is lead by ISI, with a total FFCUL contribution of 19 persons.month (12 hired + (7) academics).

Activities at FFCUL in the third semester of the project in this work package:

- Mário Silva and Fabrício Silva participated in the Project Review in Brussels, March 2010
- Mário Silva and Fabrício Silva attended the COSI-ICT cluster workshop in Brussels, March 2010
- Discussions in Amsterdam, May 2010.

- Validation of the meta-data uploaded by ISI, discussions on how EM data would be accessed from the computational platform tools and support in the process.

4.1 Effort Allocation

The effort allocated to WP4 in the reporting period is as follows:

WP4 FFCUL **Reporting Period**	**Effort (p.m)** Perm + Non-perm =Total
Year 1: February 1, 2009 to January 31, 2010	5.72+0.50 = 6.22
Semester 3: February 1, 2010 to July 31, 2010	3.30 + 0.24 = 3.54

The commitment to the project in the first year was 6.22 persons.month, 5.72 pm from technicians, and 0.50 p.m from permanent staff.

The commitment to the project in the third semester (the reporting period) was 3.54 persons.month, 3.30 pm from technicians, and 0.24 p.from permanent staff.

This is as planned, reflecting the fact that this task is led by ISI and our contribution will intensify later, as we settle on a common software architecture, including interfaces, for orchestrating and running services on both platforms. The reported effort by technicians reflects the splitting of the effort dedicated to setting-up the hardware and base software of the epiwork infrastrucure in Lisbon between WP3 and WP4.

5 Work in WP7 — Management

This task is lead by ISI.

FFCUL Effort in this task: 4 persons.month.

Activities at FFCUL in the third semester of the project in this work package:

1. Mário Silva and Fabricio Silva attended the Epiwork Review in Brussels, March 2010.
2. Data collection activities for preparation of the 3rd semester report and this interim report.

5.1 Effort Allocation

The effort allocated to WP7 in the reporting period is as follows:

WP7 FFCUL **Reporting Period**	**Effort** (p.m) Perm + Non-perm =Total
Year 1: February 1, 2009 to January 31, 2010	1.10 + 0.0 = 1.10
Semester 3: February 1, 2010 to July 31, 2010	0.42 + 0.0 = 0.42

The effort dedicated to the project in the period, 0.42 p.m., was 100% contributed by permanent staff, as planned.

EPIWORK, Report September 2010:

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September 13, 2010

1. Scientific background and activities: Main tasks in Workpackage 1 are modelling and parameter estimation in influenza, seasonal and pandemic, and investigation of network models for the spread of transmittable diseases like influenza and others, especially in the context of spatially restricted networks.

Predictability of outbreaks is in this context of major importance, as it can be quantified by system theories like deterministic chaos and criticality, i.e. predicion horizons given by Lyapunov exponents (especially in simple epidemic already showing large parameter regions of deterministic chaos) and large scale fluctuations of system size as observed near critical thresholds (as they become more and more relevant in evolutionary biological pathogen systems).

These basic notions are vital for the data gathering and analysis in the other work packages of the EPIWORK porject, as well as the feedback from the more applied work packages are vital for the modelling and parameter estimation part in workpackage 1.

The role of seasonality and reinfection on the description and predictability of epidemiological systems is a further task in Workpackage 1, and leads to subtle interplays between noise, extinction of a diesease in a reporting area, and reintroduction due to import from outside the region. Here, parameter estimation from data in a region and coupling to the outside, as modelled e.g. by spatially restricted networks, come together and are both needed for the understanding and eventual managing of epidemiological outbreaks.

In accordance with these premisses we from the CMAF team have performed the following activities during the reporting time Feb. to July 2010:

Since Sebastien Ballesteros has joined our group in CMAF as post-doctoral student, modelling and parameter estimation of highly non-linear epidemiological systems has been strengthened significantly. Currently, Sebastien is estimating parameters for influenza from time series from his home Ile-de-France, on which his doctoral thesis was centered, from Tel Aviv recently started with our EPIWORK project partner Lewi Stone, and pandemic data from last year's outbreak in collaboration with Brian Grenfell in Princeton (where he is right now), as well as parameter estimation on the Influenza Net data, provided by the other work packages of EPIWORK, this in collaboration Sander van Noort and Gabriela Gomes at IGC in Oeiras, also one of the EPIWORK partner groups.

Sebastien has as well started to estimate parameters from dengue time series in Thailand, the best known surveillence data in that field, for the Aguiar-Kooi-Stollenwerk model on dengue giving rise to already deterministically chaotic behaviour in wide parameter regions just from the multi-strain aspect, the more now including seasonality, as was also done in the influenza models. As opposed to influenza, no large parameter noise has to be used here due to the higher quality of the data sets (dengue hemorhagic fever DHF is a clear clinical phenomenon as opposed to influenza). The comparison between the two test cases of influenza and dengue has guided the analysis of such systems well.

Technically, the used algorithms have repetedly shown drifts to relatively simple dynamical behaviour, in contrast to the apparent largely varying fluctuations observed in the data serious. Finally, a first break-through has been reached by jointly estimating parameters from Ile-de-France and Tel Aviv, showing signs of complex transient behaviour due to the dynamical noise.

Whereas in childhood diseases the interplay between a stable period three and a chaotic saddle plays an important role in understanding the dynamic noise induced switching between state space structures (Drepper, Engbert, Stollenwerk, 1994), in influenza now we need to understand the transition between a stable period two limit cycle co-existing with another period one limit cycle acting as a saddle now, i.e. attracting from some direction and repelling into another. Details will be given in future presentations and manuscripts. This scenario limits the predicatbility of seasonal influenza, and at the same time gives hints on how to understand pandemic escapes at times.

In how far a second local maximum in the appearing likelihood functions will be of further relevance (as bifurcation parameter the import serves) in the region of "uniform phase chaotic amplitude" (UPCA) is currently under investigation.

On evolutionary aspects some progress has been reached by Philip Gerrish in collaboration with Claudia Ferreira during long term work visit:

The zoonotic potential of Influenza virus presents one of the greatest threats to public health, yet surprisingly little is known about the evolutionary and ecological factors that may set the stage for zoonotic events. In Influenza virus, there are two genes encoding for surface proteins exposed to immune surveillance and hence subject to rapid evolutionary change; generally speaking, these two genes can tolerate significant change and are not conserved over time. By contrast, the rest of the Influenza genes experience much less exposure to immune surveillance and encode for proteins whose functions are more essential and must therefore be conserved over time to insure the continued replication of the virus; these genes are commonly referred to as housekeeping genes. A subset of such housekeeping genes code for the viral replication complex, which is composed of the three polymerase subunits (PB2, PB1, and PA) and the nucleoprotein; this complex is now recognized as a determinant of virulence and pathogenicity. The most prominent example is the amino acid at position 627 of the PB2 protein: briefly, Lys at this position results in high pathogenicity of H5N1 viruses in mammalian species, whereas Glu at this position renders viruses low pathogenic in mammalian species. In recent studies of a highly pathogenic H5N1 strain of avian influenza virus, we have observed the evolutionary rearrangement and de novo assembly of a novel configuration of viral housekeeping genes (including the replication complex), followed by a divergence of this virus into three lineages with disparate evolutionary trajectories even to the point of acquiring a degree of between-lineage hybrid incompatibility. Careful study of these lineages may provide an unprecedented opportunity to study the viral ecology and evolution that give rise to the kind of punctuated evolutionary events we have observed, the propensity for divergence, and perhaps their pre-

disposition for zoonoses. To date, most of our thinking and discussions have focused on viral evolution, and we have not given much consideration to the ecology of the virus a bias that is reflected in our mathematical models.

Dr. Ferreira has done considerable work studying the impact of ecology on evolutionary patterns of infectious diseases, and her experience will bring a new and essential perspective to our endeavors. From phylogenetic analysis of the nucleotide sequence of influenza A virus RNA segments coding for the spike proteins (HA, NA, and M2) and the internal proteins (PB2, PB1, PA, NP, M, and NS) from a wide range of hosts, geographical regions, and influenza A virus subtypes, the following observations have been made: (i) Two partly overlapping reservoirs of influenza A viruses exist in migrating waterfowl and shorebirds throughout the world. These species harbor influenza viruses of all the known HA and NA subtypes. (ii) Influenza viruses have evolved into a number of host-specific lineages that are exemplified by the NP gene and include equine Prague/56, recent equine strains, classical swine and human strains, H13 gull strains, and all other avian strains. Other genes show similar patterns, but with extensive evidence of genetic reassortment. Geographical as well as host-specific lineages are evident. (iii) All of the influenza A viruses of mammalian sources originated from the avian gene pool, and it is possible that influenza B viruses also arose from the same source. (iv) The different virus lineages are predominantly host specific, but there are periodic exchanges of influenza virus genes or whole viruses between species, giving rise to pandemics of disease in humans, lower animals, and birds. (v) The influenza viruses currently circulating in humans and pigs in North America originated by transmission of all genes from the avian reservoir prior to the 1918 Spanish influenza pandemic; some of the genes have subsequently been replaced by others from the influenza gene pool in birds. (vi) The influenza virus gene pool in aquatic birds of the world is probably perpetuated by low-level transmission within that species throughout the year. (vii) There is speculation that pigs may serve as the intermediate host in genetic exchange between influenza viruses in avian and humans, but experimental evidence is lacking. (viii) Once the ecological properties of influenza viruses are understood, it may be possible to interdict the introduction of new influenza viruses into humans. Dr. Ferreira will investigate the H5N1 strain, whose punctuated evolution and divergence we have observed, in light of the foregoing ecological considerations. Also, she hopes to investigate the role of ecology in determining whether the primary mode of viral evolution is through recombination or mutation a question of central relevance to our current project.

The basic role of reinfection on spatially extended epidemiological systems has been investigated for a while by the groups in CMAF and in Oeiras. A summarizing publication has been recently accepted, with authors from EPIWORK: Nico Stollenwerk, Frank Hilker, Sander van Noort and Gabriela Gomes and further participating researchers. This is basis for further investiagtions into spreading mechanisms, like spatially restricted networks, when it comes to considering waning immunity and reinfection together.

Some of the above mentioned research activities together with results from the previous EPWORK year have been presented to the international scientific community:

The CMAF group has organized in February a workshop at Lisbon University with the participation of 50 colleagues, DSABN 2010.

We are currently organizing the second edition DSABN 2011, planed for Feb. 2 to 4, 2011, again at Lisbon University, with an already well going list of international speakers.

The 2010 edition of DASBN was held 1. to 3. of February 2010 as "Dynamical Systems Applied to Biology and Natural Sciences (DSABN 2010)" at CMAF with more than 50 participants from Italy, France, Netherlands, UK, India, Brazil, USA, Check Republic and Portugal with strong participation from EPIWORK members (all CMAF members: Frank Hilker, Philip Gerrish, Sebastien Ballesteros, Nico Stollenwerk, all presenting talks and posters, further EPIwork members presenting talks were Gabriela Gomes, who gave the word to Sander van Noort, and Flavio Coelho). Topics from these and further speakers were among others epidemic modelling and data analysis of influenza and vector borne diseases, pathogen evolution, and mathematiccal techniques applicable to epidemiological and ecological modelling. (see http://ptmat.fc.ul.pt/ dsabn2010/)

We organized one conference special session at the international conference CMMSE in Almeria, Spain in June 2010, as a follow up from the previous CMMSE in Gijon in 2009. Published references of the conference contributions see below. Participants from the EPIWORK members of CMAF were Philip Gerrish, Sebastien Ballesteros and Nico Stollenwerk, with further participants from CMAF, linked thematically to the ongoing research of EPIWORK.

We are currently organizing another special session at an international conference ICNAAM 2010, which will be held in September 2010 in Rhodos, Greece, in collaboration with University Torino. Conference contributions are accepted for the proceedings, and will be eligible to publication in international journals. References will be given below.

Further participation in international conferences were, among others, Sebastien Ballesteros and Nico Stollenwerk (invited talks) at a workshop in Carghese, France, and CMPD 3 in Bordeaux, France, with Sebastien Ballesteros, Frank Hilker and Nico Stollenwerk. CMPD 3 was a huge success in ringing most internationally known mathematical biologists together.

Nico Stollenwerk joint the EPIWORK team during the first year evaluation in Brussles in March 2010 and presented results together with Lewi Stone on WP1.

References

Publications in refereed international journals:

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